Remarks:

The executed Declaration of Kenneth Walsh under 37 C.F.R. 1.131 was mailed to the USPTO on December 6, 2002. In a telephone message left for the undersigned attorney, the Examiner indicated that he had located the executed Declaration in the file.

As noted in the first paragraph of this response, it is the understanding of the undersigned attorney that the Examiner intends to cancel the January 15, 2002 Office Action and to issue a NEW Final Office Action that will take into account the executed Declaration of K. Walsh. It further is the understanding of the undersigned attorney that the Examiner will delineate the specific deficiencies in the response submitted herewith to facilitate the preparation of a further Declaration by K. Walsh which addresses any unresolved issues relating to Dr. Walsh's date of invention compared to the cited prior art including, for example, inclusion of the attorney explanation of the Walsh declaration evidence into a further declaration by Dr. Walsh. The Examiner's efforts to further the prosecution of this application are greatly appreciated.

Rejection under 35 U.S.C. 103(a)

Claims 1-4 remain rejected under 35 U.S.C. 103(a) "as being unpatentable over Cuevas et al. Eur.J.Med.Res, Vol.2, pages 465-468, November, 1997) in view of Datta et al. (Cell, Vol.91, pages 231-241, October, 1997) for the reasons of record". Claim 5 remains objected to for the reasons of record. The Examiner has not found Applicant's Declaration and prior response persuasive for the following reasons:

1. The Declaration does not establish a date of conception of the invention prior to October 17, 1997, which is the publication date appearing on the S. Datta et al. reference.
2. The Declaration does not establish due diligence in reducing the invention to practice from a date prior to the publication date of the Datta et al. reference. In particular, the Declaration evidence does not establish that Akt inhibits apoptotic cell-death but instead, measure VEGF stimulation in endothelial cells.
3. The Declaration is unsigned.

Applicant respectfully traverses this rejection for the reasons of record and in view of the further explanation of the Walsh Declaration evidence which follows.

The purpose for filing the Walsh Declaration evidence was to remove the Datta et al. reference as prior art against the pending claims.

The Datta et al. reference is dated October 17, 1997.

The pending application claims priority to a provisional application filed October 2, 1998. The pending application is substantially identical to the priority document. Accordingly, Applicant may submit evidence in the form of a 1.131 Declaration to establish a date of invention as early as October 2, 1997. If Applicant can establish a date of conception prior to the Datta et al. reference date (October 17, 1997), Applicant can remove the Datta reference as prior art against the pending claims.

The Walsh Declaration Exhibit A includes evidence from November 1997 that Akt inhibits apoptotic cell-death of myocytes.

The Examiner is correct in stating that the Declaration, Exhibit A describes the results of experiments that were performed in November 1997. Exhibit A describes the results of experiments which establish that Akt inhibits apoptotic cell-death of myocytes. The application as filed includes the Exhibit A strategy and results (Example 1 of the pending application). The Walsh Declaration Exhibit A evidence establishes a date of conception *at least as early* as November 1997; however, this evidence *alone* is insufficient to swear behind the Datta et al. reference. The Walsh Declaration Exhibit B evidence was submitted to supplement the Exhibit A evidence by showing an even earlier date of conception based on results obtained using endothelial cells and diligence in reduction to practice until the filing of Applicant's priority provisional application. The Exhibit B evidence is discussed below.

The Walsh Declaration Exhibit B includes evidence from April 1996 that Akt promotes endothelial cell viability in response to VEGF.

The pending application describes the ability of Akt to promote endothelial cell viability in response to VEGF (see page 43)":

> "To further explore the functional significance of VEGF-induced Akt activity in endothelial cell survival, a replication-defective adenoviral vector expressing wild-type Akt (Ad-Akt) was constructed (Fig. 3A). Control cultures were infected with an adenoviral vector expressing ß-galactosidase (Ad- ß-gal), which does not affect

endothelial cell viability under the conditions of our assay. As shown in Fig. 3B, adenoviral transfection of Akt markedly augmented VEGF-induced endothelial cell survival. ...These data show that forced Akt expression can enhance the sensitivity of endothelial cells to VEGF survival signals."

The Walsh Declaration Exhibit B includes the results of experiments which correspond to those described in Example 2 of the application as filed (see pages 40-43 and figures 3A and 3B). In particular, the Walsh Declaration Exhibit B results show that Akt expression can enhance the sensitivity of endothelial cells to VEGF survival signals as also shown in figure 3B of the application as filed. Copies of the application Fig. 3B and the Walsh Declaration Exhibit B figure are attached to facilitate the Examiner's comparison of these results.

The pending application describes and claims a method for treating myocardial infarction that involves administering an Akt molecule in an amount to inhibit cardiac tissue necrosis in the subject wherein the tissue necrosis can be mediated by increased death of cardiomyocytes or by increased death of cardiac tissue endothelial cells.

As noted in the Summary of the Invention (page 2, emphasis added):

"The invention involves the discovery that Akt ... inhibits apoptotic cell-death of cells, and in particular, inhibits apoptotic cell-death of cardiomyocytes, skeletal myocytes and/or vascular endothelial cells. In view of these discoveries, it is believed that Akt molecules can be used to inhibit apoptotic cell-death of the afore-mentioned cell types, and in particular, to treat conditions (e.g., myocardial infarction) that result in increased apoptotic cell-death of cardiomyocytes, skeletal myocytes and/or vascular endothelial cells."

The pending claims are directed to a method for treating myocardial infarction "by administering to a subject ... an Akt molecule in an amount effective to inhibit cardiac tissue necrosis in the subject" (claim 1). The dependent claims include further limitation directed to characterizing the cardiac tissue necrosis, namely, that it is "mediated by increased apoptotic cell-death of a cardiomyocyte" (claim 2) or that it is "mediated by increased apoptotic cell-death of a cardiac tissue endothelial cell" (claim 3).

In summary, the Walsh Declaration provides evidence of the ability of Akt to promote endothelial cell viability in response to VEGF (Exhibit B) from a date at least as early as April 1996 and evidence that Akt inhibits apoptotic cell-death of myocytes from at least as early as

November 1997. Applicant believes that this evidence should be sufficient to establish conception and diligence in reduction to practice of the claimed invention as of a date prior to October 17, 1997, which is the publication date appearing on the Datta et al. reference.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-4 under 35 U.S.C. §103(a) in view of the cited art.

Claim Objection:

Claim 5 is objected to as being dependent upon a rejected base claim. Applicants appreciate that the Examiner has found the claim 5 allowable over the prior art of record; however, Applicants have elected not to rewrite this claim in independent form in view of the previously-submitted arguments in favor of the patentability of the base claim and the explanation of the Walsh Declaration submitted herewith.

Summary:

As previously noted, it is the undersigned attorney's understanding that the outstanding Final Office Action will be cancelled and a new Final Office Action issued.

Applicants believe that each of the pending claims now is in condition for allowance. Applicants respectfully request that the Examiner telephone the undersigned attorney in the event that the claims are not found to be in condition for allowance.

If the Examiner has any questions and believes that a telephone conference with Applicant's attorney would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at (617) 720-3500 (extension 343).

Respectfully submitted,

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